



Complete Summary

GUIDELINE TITLE

Syphilis.

BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Syphilis. In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2006 Jul 25 [Various].

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Reunala T. Syphilis. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2004 Jun 19 [various].

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [September 11, 2007, Rocephin \(ceftriaxone sodium\)](#): Roche informed healthcare professionals about revisions made to the prescribing information for Rocephin to clarify the potential risk associated with concomitant use of Rocephin with calcium or calcium-containing solutions or products.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **

SCOPE

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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT

CATEGORIES

IDENTIFYING INFORMATION AND AVAILABILITY

DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Syphilis, including:

- Primary, secondary, and latent syphilis
- Neurosyphilis
- Syphilis in pregnancy
- Congenital syphilis (prevention)
- Neonatal syphilis (diagnosis)

GUIDELINE CATEGORY

Diagnosis
Management
Prevention
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Obstetrics and Gynecology
Pediatrics

INTENDED USERS

Health Care Providers
Physicians

GUIDELINE OBJECTIVE(S)

Evidence-Based Medicine Guidelines collect, summarize, and update the core clinical knowledge essential in general practice. The guidelines also describe the scientific evidence underlying the given recommendations.

TARGET POPULATION

Patients with suspected or confirmed syphilis and patients exposed to syphilis

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Assessment of history of exposure and signs and symptoms of syphilis
2. Microscopic assessment of lesion discharge for spirochetes
3. Serologic testing (cardiolipin test, Treponema pallidum haemagglutination test [TPHA], fluorescent treponemal antibody absorption [FTA-abs] test as indicated for special cases)

4. Gene amplification methods for screening

Management/Treatment/Prevention

1. Penicillin for the treatment of primary, secondary and latent syphilis, neurosyphilis, and syphilis in pregnancy, and the prevention of congenital syphilis
2. Ceftriaxone injections as alternative for patients who are allergic to penicillin
3. After completion of antibiotic treatment, follow-up testing with the cardiolipin and Treponema pallidum haemagglutination tests at specified intervals
4. Identification and screening of partners with cardiolipin test

MAJOR OUTCOMES CONSIDERED

- Accuracy of diagnostic tests
- Incidence of congenital syphilis
- Rate of referral of sex partners
- Signs and symptoms of syphilis
- Syphilis serology titers

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The evidence reviewed was collected from the Cochrane database of systematic reviews and the Database of Abstracts of Reviews of Effectiveness (DARE). In addition, the Cochrane Library and medical journals were searched specifically for original publications.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

- A. Strong research-based evidence. Multiple relevant, high-quality scientific studies with homogeneous results.

- B. Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.
- C. Limited research-based evidence. At least one adequate scientific study.
- D. No research-based evidence. Expert panel evaluation of other information.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence [A-D] supporting the recommendations are defined at the end of the "Major Recommendations" field.

Aims

- Suspected syphilis should be verified with the appropriate clinical and serological tests and the patient should be treated with the most efficient antibiotics.
- Syphilis is a dangerous infectious disease that should be prevented and treated effectively.

Aetiology and Transmission

- The pathogen is the spirochete *Treponema pallidum*.
- Easily transmitted by sexual intercourse and also from the mother to the foetus.
- Contagiousness is highest (30–60%) in the primary and secondary phases. After 2 years, the patient ceases to spread the disease.

Clinical Picture

- Asymptomatic incubation period lasts for 3 to 4 weeks after which two thirds of the patients (not all) have visible symptoms
 1. Primary symptoms (local infection)
 - An ulcer, the "primary lesion," with a clean, hard base (see picture 1*) appears in the genital region, sometimes also in anus or the oral region.
 - There is local lymphadenopathy without tenderness.
 2. Secondary stage 6 to 8 weeks after exposure (general infection).
 - General symptoms include indisposition, fever and enlarged lymph nodes.
 - Roseola eczema (see picture 2*) resembles widely spread viral eczema or drug eruption.
 - Syphilids (i.e., formations of papules) are found in the hands and feet or spread all over the body. May be large, cauliflower-like formations (condylomata latum) around the anus or necrotic in patients with a poor immune response (e.g. human immunodeficiency virus [HIV])
 - Alopecia syphilitica, typical "moth-eaten" spotty baldness in some patients
 3. Late symptoms occur in about one third of untreated patients in 10 to 30 years. The most important are neurological (atypical psychosis, paralytic dementia) and vascular symptoms (aortic aneurysm, valvular regurgitation).

Differential Diagnosis

- Primary syphilis
 - Genital herpes. Incubation time is short in primary infection, lesions occur in groups and they are painful. Lymphadenopathy is less pronounced; however, the nodes are tender.
 - Ulcus molle (soft chancre)
 - Infected coital or other traumas
- Secondary syphilis
 - Roseola may resemble pityriasis rosea, drug eruption, measles (rubeola), German measles (rubella), or scarlet fever (scarlatina).
 - Syphilids may resemble papular lichen ruber planus, psoriasis, scabies or infectious eczema of the feet (e.g., tinea). Condyloma latum may resemble condyloma acuminata.

Diagnosis

1. History of exposure (unprotected sex) and/or clinical picture.
2. Plain specimen. A dark field microscope may reveal spirochetes in lesion discharge and confirm the diagnosis.
3. Serology
 - The cardiolipin test becomes positive 3 to 4 weeks after infection. It is the primary test for screening. High titres (>16) are almost always specific. A low titre is in many cases a false positive result (pregnancy, connective tissue disease, infection) or a serological scar of an earlier treated infection or latent syphilis.
 - Treponema pallidum haemagglutination test (TPHA) is the test of choice for verifying syphilis. The result becomes positive slightly later than that of the cardiolipin test, but it is specific (almost 100%) and suitable for following up response to treatment.
 - Fluorescent treponemal antibody absorption test (FTA-abs) is a specific syphilis test used in special cases (neurosyphilis, suspicion of neonatal syphilis) as it detects also immunoglobulin M (IgM) antibodies.
 - Gene amplification methods are already being used for screening.

Treatment

- Procaine penicillin 1.2 million IU x 1 intramuscular (i.m.) for 10 days (primary and secondary syphilis; in latent syphilis treatment is received for three weeks), in neurosyphilis intravenous (i.v.) penicillin.
- For patients allergic to penicillin, ceftriaxone injections (1 g/day) are an alternative.

Follow-up and Identification of Partners

- After antibiotic therapy the cardiolipin and treponema pallidum haemagglutination tests are performed at 3 and 6 months and one year. In primary stage infection, the tests become negative in most cases; in other recent infections the titre falls by at least two dilutions when the treatment has been successful.
- All sexual partners who have been exposed to infection should be screened with the cardiolipin test. If the result is negative, the test should be repeated after 3 months.

Related Evidence

- Patient assistance at facilitating patient referral and provider referral may increase partner notification for sexually transmitted diseases (Oxman et al., 1994) [C].
- Penicillin is effective in the treatment of syphilis in pregnancy and in the prevention of congenital syphilis (Walker, 2001) [B].

*Note: All pictures identified in this summary can be found in the original guideline document (see "Guideline Availability" field).

Definitions:

Levels of Evidence

- A. Strong research-based evidence. Multiple relevant, high-quality scientific studies with homogeneous results.
- B. Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.
- C. Limited research-based evidence. At least one adequate scientific study.
- D. No research-based evidence. Expert panel evaluation of other information.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

[References open in a new window](#)

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Concise summaries of scientific evidence attached to the individual guidelines are the unique feature of the Evidence-Based Medicine Guidelines. The evidence summaries allow the clinician to judge how well-founded the treatment recommendations are. The type of supporting evidence is identified and graded for select recommendations (see the "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate use of clinical and serological tests for the verification of suspected syphilis
- Effective prevention and treatment of syphilis

POTENTIAL HARMS

The cardiolipin test is the primary test for screening. High titres (>16) are almost always specific. A low titre is in many cases a false positive result (pregnancy, connective tissue disease, infection) or a serological scar of an earlier treated infection or latent syphilis.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Syphilis. In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2006 Jul 25 [Various].

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 Nov 22 (revised 2006 Jul 25)

GUIDELINE DEVELOPER(S)

Finnish Medical Society Duodecim - Professional Association

SOURCE(S) OF FUNDING

Finnish Medical Society Duodecim

GUIDELINE COMMITTEE

Editorial Team of EBM Guidelines

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Author: Timo Reunala

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

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This guideline updates a previous version: Reunala T. Syphilis. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2004 Jun 19 [various].

GUIDELINE AVAILABILITY

This guideline is included in "EBM Guidelines. Evidence-Based Medicine" available from Duodecim Medical Publications, Ltd, PO Box 713, 00101 Helsinki, Finland; e-mail: info@ebm-guidelines.com; Web site: www.ebm-guidelines.com.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on December 17, 2002. The information was verified by the guideline developer on February 7, 2003. This NGC summary was updated by ECRI on October 4, 2004 and on December 22, 2006. This summary was updated by ECRI Institute on October 3, 2007 following the U.S. Food and Drug Administration (FDA) advisory on Rocephin (ceftriaxone sodium).

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